

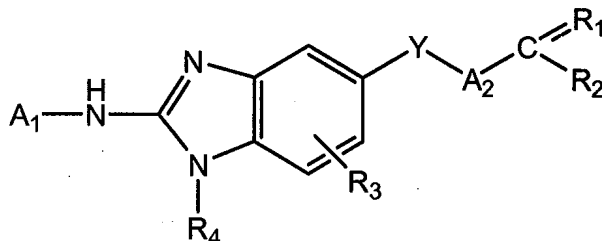
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

1-74. (Canceled)

75. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated cancer disorder selected from the group consisting of melanoma, breast cancer, prostate cancer, lung cancer, pancreatic cancer, thyroid cancer, bladder cancer, colon cancer, liver cancer, myeloid leukemia, and villous colon adenoma, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (II) effective to inhibit Raf kinase activity in the human or animal subject:



(II)

wherein Y is O;

A₁ is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

~~A₂ is substituted or unsubstituted heteroaryl;~~

~~R₁ is O or H, and R₂ is NR₅R₆ or hydroxyl; or R₁ is taken together with R₂ to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;~~

~~R₃ is hydrogen, halogen, loweralkyl, or loweralkoxy; and~~

~~R₄ is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl; [[and]]~~

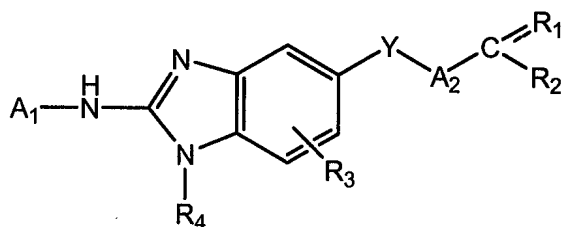
~~R₅ and R₆ are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R₅ and R₆ are taken together to form substituted or unsubstituted heterocyclo or heteroaryl;~~

~~or a pharmaceutically acceptable salt thereof.~~

76. (Previously presented) The method of claim 75 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

77. (Canceled)

78. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated hormone dependent cancer disorder selected from the group consisting of breast cancer and prostate cancer, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (II) effective to inhibit Raf kinase activity in the human or animal subject:



(II)

wherein Y is O;

~~A₁ is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;~~

~~A₂ is substituted or unsubstituted heteroaryl;~~

~~R₁ is O or H, and R₂ is NR₅R₆ or hydroxyl; or R₁ is taken together with R₂ to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;~~

~~R₃ is hydrogen, halogen, loweralkyl, or loweralkoxy; and~~

~~R₄ is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl; [[and]]~~

~~R₅ and R₆ are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R₅ and R₆ are taken together to form substituted or unsubstituted heterocyclo or heteroaryl;~~

or a pharmaceutically acceptable salt thereof.

79. (Canceled)

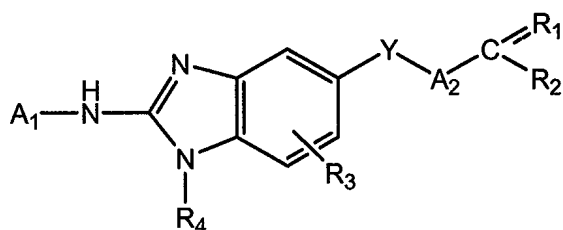
80. (Previously presented) The method of claim 78 which further comprises administering to the human or animal subject at least one additional agent for the treatment of

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

81. (Canceled)

82. (Currently amended) A method of inhibiting Raf kinase activity in a human or animal subject suffering from a Ras/mitogen-activated protein kinase signal pathway-mediated hematological cancer disorder, comprising administering to the human or animal subject a composition comprising an amount of a compound of the formula (II) effective to inhibit Raf kinase activity in the human or animal subject:



(II)

wherein Y is O;

A₁ is substituted or unsubstituted alkyl, cycloalkyl, heterocycloalkyl, aryl, polycyclic aryl, polycyclic arylalkyl, heteroaryl, biaryl, heteroarylaryl, heteroarylheteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, biarylalkyl, or heteroarylarylalkyl;

A₂ is substituted or unsubstituted heteroaryl;

R₁ is O or H, and R₂ is NR₅R₆ or hydroxyl; or R₁ is taken together with R₂ to form a substituted or unsubstituted heterocycloalkyl or heteroaryl group; wherein, the dashed line represents a single or double bond;

R₃ is hydrogen, halogen, loweralkyl, or loweralkoxy; and

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

~~R₄ is hydrogen, hydroxyl, alkylamino, dialkylamino or alkyl; [[and]]~~

~~R₅ and R₆ are independently selected from hydrogen, and substituted or unsubstituted alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkyloxyalkylheterocyclo, and heteroarylalkyl; or R₅ and R₆ are taken together to form substituted or unsubstituted heterocyclo or heteroaryl;~~

or a pharmaceutically acceptable salt thereof.

83. (Previously presented) The method of claim 82 which further comprises administering to the human or animal subject at least one additional agent for the treatment of cancer selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab and trastuzumab.

84-87. (Canceled)

88. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₄ in formula (II) is ~~hydrogen or~~ C₁₋₆ alkyl.

89. (Previously presented) The method of claim 88, wherein R₄ in formula (II) is methyl.

90. (Canceled)

91. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A₁ in formula (II) is a substituted or unsubstituted C₃₋₁₄ aryl carbocyclic aryl group.

92. (Currently amended) The method of claim ~~[[91]]~~ 75, wherein A₁ in formula (II) is selected from the group consisting of substituted ~~or unsubstituted~~ phenyl, pyridyl, pyrimidinyl,

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

~~phenylalkyl, pyridylalkyl, pyrimidinylalkyl, heterocyclylcarbonylphenyl, heterocyclylphenyl, heterocyclylalkylphenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkylbenzoate, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, thiophene, thiophenyl, thiophene-2-carboxylate, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, indenyl, 2,3-dihydroindenyl, tetralinyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, morpholinyl, N-piperazinyl, N-morpholinylalkyl, piperazinylalkyl, cyclohexylalkyl, indolyl, 2,3-dihydroindolyl, 1-acetyl-2,3-dihydroindolyl, cycloheptyl, bicyclo[2.2.1]hept-2-yl, hydroxyphenyl, hydroxyalkylphenyl, pyrrolidinyl, pyrrolidin-1-yl, pyrrolidin-1-ylalkyl, 4-amino(imino)methylphenyl, isoxazolyl, indazolyl, adamantyl, bicyclohexyl, quinuclidinyl, imidazolyl, benzimidazolyl, imidazolylphenyl, phenylimidazolyl, phthalamido, naphthyl, benzophenone, anilinyl, anisolyl, quinolinyl, quinolinonyl, phenylsulfonyl, phenylalkylsulfonyl, 9H-fluoren-1-yl, piperidin-1-yl, piperidin-1-ylalkyl, cyclopropyl, cyclopropylalkyl, pyrimidin-5-ylphenyl, quinolidinylphenyl, or furanyl, furanylphenyl, N-methylpiperidin-4-yl, pyrrolidin-4-ylpyridinyl, 4-diazepan-1-yl, hydroxypyrrolidin-1-yl, dialkylaminopyrrolidin-1-yl, 1,4'-bipiperidin-1'-yl, and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.~~

93. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A₁ in formula (II) is selected from the group consisting of ~~substituted or unsubstituted phenyl,~~ chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl,

alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, hydroxyphenyl, hydroxyalkylphenyl, 4-amino(imino)methylphenyl and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

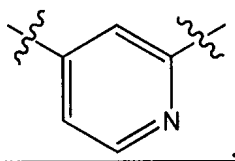
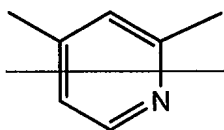
94. (Previously presented) The method of claim 93, wherein A₁ in formula (II) is 4-bromophenyl.

95. (Previously presented) The method of claim 93, wherein A₁ in formula (II) is trifluoromethylchlorophenyl.

96. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein A₂ in formula (II) is selected from the group consisting of ~~substituted or unsubstituted phenyl~~, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinolinyl, purinyl, ~~naphthyl~~, benzothiazolyl, benzopyridyl and benzoimidazolyl.

97. (Currently amended) The method of claim 96, wherein A₂ in formula (II) is unsubstituted pyridyl.

98. (Currently amended) The method of claim 96, wherein A₂ in formula (II) is



99. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₁ is taken together with R₂ in formula (II) to form a substituted ~~or unsubstituted C₃₋₈ heterocycloalkyl~~ or C₃₋₁₄ heteroaryl group, wherein the C₃₋₁₄ heteroaryl group contains only carbon and nitrogen atoms as ring atoms.

100. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₁ is taken together with R₂ in formula (II) to form a group selected from substituted ~~or unsubstituted phenyl~~, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinoliny, purinyl, ~~naphthyl~~, benzothiazolyl, benzopyridyl and benzoimidazolyl.

101. (Currently amended) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein R₁ is taken together with R₂ in formula (II) to form a substituted ~~or unsubstituted~~ imidazolyl group.

102. (Previously presented) The method of claim 100, wherein the imidazolyl group is substituted with a halo C₁₋₆ alkyl group.

103. (Previously presented) The method of claim 100, wherein the imidazolyl group is substituted with a trifluoromethyl group.

104-107. (Canceled)

108. (Previously presented) The method of claim 75, wherein the cancer is melanoma.

109. (Previously presented) The method of claim 75, wherein the cancer is a carcinoma of the lungs, pancreas, thyroid, bladder or colon.

110. (Previously presented) The method of claim 75, wherein the cancer is myeloid leukemia.

111. (Previously presented) The method of claim 75, wherein the cancer is villous colon adenoma.

112. (Previously presented) The method of claim 82 wherein the hematological cancer disorder is chronic myelogenous leukemia.

113. (New) The method of claim 75, wherein A₁ in formula (II) is selected from the group consisting of phenylalkyl, pyridylalkyl, pyrimidinylalkyl, heterocyclcarbonylphenyl, heterocyclphenyl, heterocyclalkylphenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, dihalophenyl, nitrophenyl, 4-bromophenyl, 4-chlorophenyl, alkylbenzoate, alkoxyphenyl, dialkoxyphenyl, dialkylphenyl, trialkylphenyl, thiophene-2-carboxylate, alkylthiophenyl, trifluoromethylphenyl, acetylphenyl, sulfamoylphenyl, biphenyl, cyclohexylphenyl, phenyloxyphenyl, dialkylaminophenyl, alkylbromophenyl, alkylchlorophenyl, alkylfluorophenyl, trifluoromethylchlorophenyl, trifluoromethylbromophenyl, 2,3-dihydroindenyl, tetralinyl, trifluorophenyl, (trifluoromethyl)thiophenyl, alkoxybiphenyl, indolyl, 2,3-dihydroindolyl, 1-acetyl-2,3-dihydroindolyl, hydroxyphenyl, hydroxyalkylphenyl, 4-amino(imino)methylphenyl, imidazolylphenyl, phenylimidazolyl, pthalamido, benzophenone, anilinyl, anisolyl, quinolinonyl, phenylsulfonyl, phenylalkylsulfonyl, pyrimidin-5-ylphenyl, quinolidinylphenyl, furanylphenyl, pyrrolidin-4-ylpyridinyl, and (1,4'-bipiperidin-1'-ylcarbonyl)phenyl.

114. (New) A method of any one of claims 75, 76, 78, 80, 82, or 83, wherein the variables in formula (II) are as follows:

A₁ is a substituted carbocyclic aryl group;

A₂ is unsubstituted pyridyl;

R₁ is taken together with R₂ to form a substituted C₃₋₁₄ heteroaryl group, wherein the C₃₋₁₄ heteroaryl group contains only carbon and nitrogen atoms as ring atoms; and

R₄ is C₁₋₆ alkyl;

or a pharmaceutically acceptable salt thereof.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100